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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/602,272	02/16/1996	MICHAEL J. ELLIOTT	KIR96-01	4297

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EXAMINER	
CANELLA, KAREN A	
ART UNIT	PAPER NUMBER
1643	
MAIL DATE	DELIVERY MODE
11/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** t00	**Applicant(s)** ELLIOTT ET AL.	
	Examiner Karen A. Canella	**Art Unit** 1643	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 October 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): none.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: *51*.
   Claim(s) objected to: *none*.
   Claim(s) rejected: *6,9,10,12-15 and 53*.
   Claim(s) withdrawn from consideration: *none*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Karen A Canella/
Primary Examiner, Art Unit 1643

Continuation of 11. does NOT place the application in condition for allowance because: The arguments fail to overcome the rejections of record. Applicant argues that Le et al fails to teach an anti-TNF antibody which would be effective in the rat model of Strieter et al. This is not persuasive. The teachings of Strieter et al relied upon for the rejection were that of the suggestion in the abstract that administration of anti-TNF antibodies may limit organ damage and decrease mortality rate in diseases including ischemia-reperfusion injury. One of skill in the art upon reading of said abstract would not infer that Strieter et al was limiting this suggestion to the treatment of experimental rat models. Applicant argues that the antibody of Le et al does not neutralize murine TNF. This is unpersuasive. Le et al teach that although mAb A2 or cA2 does not inhibit or neutralize human lymphotoxin (page 11, lines 12-13), but the inhibition or neutralization of lymphotoxin but this is not required by the instant claims., Le et al does teach that mAb A2 inhibits recombinant human TNF-alpha (page 6, lines 16-18) which is the TNF specified in the instant claims. Let al al specifically teach inhibition and neutralization of human TNF alpha in vivo (page 7, lines 21-28 Applicant further argues that the examiner incorrectly discounted the teachings of Freeman and Natanson et al stating that the examiner did not explain why using a different anti-TNF antibody than that of the Bay-X-1351 was relevant to the the discounting of the argument. This has been considered but not found persuasive. It is noted that it is the teachings of Le et al that indicate that the A2 and the cA2 antibody are improved over the prior art because it provides increased neutralization activity and the cA2 antibody provides decreased immunogenicity (page 6, line 35 to page 7, line 17). Le et al specifically state that because the circulating levels of TNF are extremely low, even in septic patients who have levels in the range of picograms/ml, it is preferable to use high affinity antibodies and/or potent in vivo TNF inhibiting or neutralizing antibodies in the therapy of TNF mediated pathologies (page 13, lines 19-28). Thus, one of skill in the art would reasonable conclude that Le et al was teaching that the affinity of the cA2 antibody would provide for a potent neutralization or inhibition of human TNF alpha in vivo. Applicant further argues that because Bender et al suggest that TNF is a likely mediator of myocardial infarction, stroke or circulatory shock, there was no reasonable basis for success. This has been considered but not found persuasive. To combine references, one of skill in the art needs only a reasonable expectation of success not a guarantee. The suggestion by Bender et al provides a reasonable expectation of success. Applicant argues that Naughton et al does not disclose the idiotype of neutralizing antibodies for TNF which can prevent thromboembolism. This has been considered but not found persuasive. Naughton et al is relied upon not for the identity of an idiotype of an anti-TNF antibody, but for the teachings regarding thromboembolism as a TNF-mediated disease which can be treated by anti-TNF antibodies. The idiotype of the anti-TNF antibody is that disclosed by Le et al.